A double blind comparative study of the effect of nimesulide and naproxen on postoperative pain and swelling following periradicular surgery

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Abstract

Background and objective: Pain and swelling are common postoperative complications that occur after periradicular surgery. A double blind comparative study was, therefore, designed to evaluate the effect of nimesulide and naproxen on the postoperative pain and swelling following periradicular surgery on one of the upper anterior teeth.

Methods: Sixty patients with a periapical lesion that required periradicular surgery were included in the study. They were divided into three groups according to the type of the postoperative analgesia they are going to administered.

Group I: Nimesulide administered group.

Group II: Naproxen administered group.

Group III: Placebo administered group.

Patients of each group were informed about the nature of the study and given the same shape of capsules. They are asked to assess their postoperative pain and swelling for 5 days by using the visual analogue scale (VAS).

Results: The results showed that both nimesulide and naproxen are effective in reducing the postoperative pain and swelling following periradicular surgery, and the nimesulide is found better than naproxen in this regard.

Conclusion: In this study both nimesulide and naproxen were significantly more effective than their corresponding placebo for reducing postoperative pain and swelling following periradicular surgery, but nimesulide administered group expressed significantly little pain in comparison to naproxen administered group, and the nimesulide administered group showed lesser swelling in the 2nd and 3rd postoperative day than those administered with naproxen.

Keywords: Nimesulide, Naproxen, Postoperative pain and swelling, Periradicular surgery

Introduction

Periradicular surgery may be required after failure of a root canal filling of a tooth with extensive coronal restoration and coverage. Conventional retreatment may be detrimental to such tooth as it may jeopardize the underlying core. Other indications for periradicular surgery are for teeth with developmental dental anomalies that prevent non-surgical root canal treatment, biopsy of lesion around the root, management of root perforations or fractures, root amputation, enucleating a periapical lesion where the apical third of the tooth is either involved by the disease or prevent its removal [1]. Pain and swelling are common postoperative complications that occur after periradicular surgery. The pain is mainly inflammatory in character and due to release of the inflammatory mediators like histamine, bradykinin, prostaglandins and leukotrienes following tissue injury[2]. Tissue injury can result in liberation of phospholipids present in the cell walls and, by the effect of the phospholipase A2; they are converted into arachidonic acid. The prostaglandins are formed from arachidonic acid through the effect of the cyclo-oxygenase enzyme (COX). The leukotrienes, on the other hand, are formed

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from the arachidonic acid by the effect of the lipo-oxygenase enzyme [3]. These inflammatory mediators act locally to excite and stimulate the nociceptors resulting in pain. The nociceptors themselves discharge pain producing substances like substance P which is also responsible for the postoperative pain [4]. The swelling likewise is caused by the inflammatory mediators .These mediators act on the blood vessel walls to increase its permeability allowing for extravagation of the plasma and its accumulation in the tissue spaces producing the clinical signs of oedema [5].The inflammatory mediators also stimulate the release by the peripheral nerve endings of substance P. This substance may induce plasma extravasations and oedema formation through histamine release [6]. The continued synthesis or release of these inflammatory mediators explains the prolonged inflammation, which far exceeds the initial stimulation of the dental procedure. Clinically pain reaches moderate to sever intensity by 5 hours [7], while oedema peaks by 48-72 hours postoperatively [8]. Nonsteroidal anti-inflammatory drugs are medications other than corticosteroids that inhibit prostaglandin synthetase, thereby reduce the process of inflammation, and hence reduce postoperative pain and swelling [9]. Nonsteroidal anti-inflammatory drugs are usually classified into the nonselective COX-1 and COX-2 inhibitors and the selective COX-1 and COX-2 inhibitors. It appears that Cox-1 enzyme is important for haemostatic maintenance such as platelet aggregation, and in regulation of gastric acid secretion. Inhibition of this enzyme by the nonselective non steroidal anti-inflammatory drugs can, therefore, result in gastric ulceration and bleeding disorders [10]. Nimesulide is a relatively COX-2 selective Nonsteroidal anti-inflammatory drug. Many clinical studies has shown that nimesulide is more effective than other Nonsteroidal anti-inflammatory drugs like voltaren in ameliorating postoperative pain and swelling [11]. However, nimesulide is contraindicated for patients with renal failure and those with liver diseases [12]. Naproxen, on the other hand, act by inhibition of both COX-1 and COX-2 enzymes. Several clinical studies have proved the efficacy of this drug in controlling postoperative pain and swelling and its superiority to ibuprofen in this regard [13]. However, as it inhibits COX-1, it may cause stomach and intestinal bleeding and ulcer [14].

Methods

This clinical study composed of 60 patients (34 males and 26 females) attended the department of oral and maxillofacial surgery, college of dentistry, Hawler medical university, and the department of oral and maxillofacial surgery, Rizgary teaching hospital from Jun. 2007 till Feb. 2008. Criteria for selection of the patients include:
*The patients had single non-vital upper anterior tooth associated with periapical lesion confirmed by periapical film.
*The patients were 18-45 years old and were medically fit and well.
*The patients had no medications within the past 14 days earlier than the day of surgery.
The medications that were given to the patient had been prepared by a fourth person who distributed the nimesulide, naproxen and the glucose powders among capsules of the same shape. The first group of the capsules was prepared to contain 100mg nimesulide each and put together inside a box labeled A. The second group of capsules was prepared to contain 500mg naproxen each and collected together inside a box labeled B. The third group of capsules, on the other hand, was prepared to contain glucose powder each and grouped together inside a box labeled C. Neither the surgeon nor the patient knows the content of the boxes or the capsule being taken to guarantee accurate results from the study. The patients were informed about the nature of the trial and asked to sign the prepared consent form. Each patient was given a visual analog scale (VAS) sheeting for

evaluation of pain, Table 1, and another one for evaluating the swelling Table 2, and shown how to fill in these sheets for five postoperative days.

Table 1: The visual analog scale (VAS) sheeting for evaluation of pain

Scale	Severity of Pain	Clinical Features
0	No pain	The patient feels well
1	Slight pain	If the patient is distracted he or she does not feel pain
2	Mild pain	The patient feels the pain even if concentrating on some activity
3	Sever pain	The patient is very disturbed, but nevertheless can continue with normal activities
4	Very sever pain	The patient is forced to abandon normal activities
5	Extremely sever pain	The patient must abandon every type of activity

Table 2: The visual analog scale (VAS) sheeting for evaluation of swelling

Scale	Severity of Swelling	Clinical Features
0	No swelling	The patient does not detect the slightest swelling
1	Mild swelling	The swelling is noticeable by the patient only but not affecting the appearance of the lip
2	Moderate swelling	The swelling is confined to the lip but not causing obliteration of the naso-labial fold
3	Sever swelling	The swelling is confined to the lip with obliteration of the naso-labial fold

Local anaesthesia was given by infiltration using two carpules of 2% lignocaine hydrochloride with 1:80,000 adrenaline. A three sided mucoperiosteal flap of sufficient size-was reflected to allow for adequate access with the least tension. The bone was then removed by the surgical burr to expose the lesion. When it is found that the apex of the root does not allow for complete removal of the lesion, an apicectomy was carried out and the lesion is curetted out with the surgical curette. The cavity was then irrigated clean, the canal instrumented to sound dentin and obturated with gutta percha. The wound was then irrigated out again and the diameter of the cavity thus created was measured by the use of the engineering divider. Finally the flap repositioned back and sutured with 3/0 black silk suture. The patient was then given the postoperative instructions and asked to take the medication for 5 days as twice daily with the first capsule taken one hour after completion of the surgery. Twenty out of the sixty patients involved in the study were given the medication from box A. Another twenty patients were given the medication from box B, whereas the rest twenty patients were given their medication from box C. The patients in each group were instructed to take the medication twice daily for (5) days. How to fill in the VAS sheets were then verified, and the patient asked to call by telephone should any difficulty arisen in the process of filling of the sheets provided. At the end of the trial the data collected were entered into a computer using the statistical package for social sciences (SPSS, version 11.5). Analysis of variance (ANOVA) was used to compare between the pain and swelling scores of the three groups. Student test was used to compare between pain and swelling scores of male and female. A P value of <0.05 was considered as statistically significant.

Results

1. Postoperative Pain in relation to the drug administered

Results has shown that the mean pain score of the nimesulide administered group was significantly less than the mean pain

score of the other groups ($p<0.05$). Patients of the placebo administered group expressed sever pain in the first and second postoperative days while none of the naproxen administered group complained from sever pain, Table 3.

2. Postoperative swelling in relation to the drug administered

Results showed that there were no significant differences in the swelling scores in the 1st, 4th and 5th postoperative days between nimesulide administered group and the naproxen treated group. However, results showed that there was a significant reduction in swelling in the 2nd and 3rd postoperative days of nimesulide administered group comparing with the other tow groups. On the other hand, patients of the placebo administered group expressed severe swelling in the 2nd, 3rd and 4th postoperative days while none of the naproxen administered group complained from severe swelling, Table 4.

Table3: Postoperative pain in relation to the drugs administered.

Pain scores		N	Mean	S.D	F	P
1ST day	nimesulide	20	1.550	604		
	placebo	20	3.750	.786		
	naproxen	20	2.050	.050	77.160	.000
	total	60	2.450	.143		
2nd day	nimesulide	20	1.000	458		
	placebo	20	3.500	.760		
	naproxen	20	1.700	.470	98.760	.000
	total	60	2.066	1.205		
3rd day	nimesulide	20	.600	502		
	placebo	20	3.000	.648		
	naproxen	20	1.100	,307	1215.192	.000
	total	60	1.566	1.155		
4th day	nimesulide	20	.0 5 0	223		
	placebo	20	2.300	.470		
	naproxen	20	.600	.502	157.633	.000
	total	60	.983	1.049		
5th day	nimesulide	20	.0 5 0	.000		
	placebo	20	2.300	.410		
	naproxen	20	.600	,366	197.765	.000
	total	60	.983	379		

Table 4: Postoperative swelling in relation to the drugs administered

Swelling scores		N	Mean	S.D	F	P
1ST day	nimesulide	20	.200	.410		
	placebo	20	.400	.502		
	naproxen	20	.200	.410	1.357	.000
	total	60	.266	,445		
2nd day	nimesulide	20	1.450	.458		
	placebo	20	2.750	.760		
	naproxen	20	1.800	.470	11.751	.000
	total	60	2.000	1.205		
3rd day	nimesulide	20	1.650	.489		
	placebo	20	2.800	.615		
	naproxen	20	1.900	.307	116.31	.000
	total	60	2.450	1.080		
4th day	nimesulide	20	1.200	.615		
	placebo	20	3.000	1.025		
	naproxen	20	1.250	.444	38.706	.000
	total	60	1.816	1.112		
5th day	nimesulide	20	.6500	.489		
	placebo	20	1.950	.223		
	naproxen	20	.650	.489	63.900	.000
	total	60	1.083	.743		

Discussion

The results from the present study showed that the pain experience is of short duration and reaches its maximum intensity in the same day of surgery. A significant reduction in pain occurs from 24-48 hours following surgery. By the fifth day patients reported little or no pain. Similar finding have been noted by Seymour R.A. and Walton J.G.[15]. The results also showed that the swelling is most marked after 24 hours and then diminishes over about the fifth postoperative day. Similar finding have been recorded by Pollman L. (2003)[16]. In this study both nimesulide and naproxen were significantly more effective than their corresponding placebo for reducing postoperative pain and swelling following periradicular surgery, but nimesulide administered group expressed significantly little pain in comparison to naproxen administered group. Similar result has been noted by Mollar P.L. (2000)[17]. Scott L.J. *et al* (1999)[18] made a comparative study of nimesulide, ibuprofen and naproxen in postoperative dental pain following third molar extraction, results showed similar analgesic efficacy of nimesulide to that of naproxen. Began J.V. & Anderson K. (2005)[19] made a clinical comparison of nimesulide, roficoxib and naproxen in postoperative dental pain by asking the patients to rate their pain intensity and its relief at regular intervals. It has been found that both nimesulide and naproxen are effective in the treatment of

acute pain following minor oral surgery, but nimesulide showed better results. Regarding the postoperative swelling, this study has shown that the group medicated by nimesulide and naproxen demonstrated lesser swelling than those medicated by placebo, and the nimesulide administered group showed lesser swelling in the 2nd and 3rd postoperative day than those administered with naproxen. Such results may be attributed to the use of the anti-inflammatory drugs as antibiotics have not been used in this study. This may support the hypothesis that antibiotics are not essential after minor surgical procedures as long the surgery contemplated under the surgical principles of asepsis. Regarding the amount of postoperative swellings, this study has shown no statistical significant difference between the three groups. These come in disagreement with Meyer R.A. *et al* (1998)[20] findings who found that postoperative swelling was gender-related, and that females experienced more swelling than the males.

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